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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/673,054	09/26/2003	Laurie Engel	02-1031-A	1228
20306 7590 01/30/2007 MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP 300 S. WACKER DRIVE 32ND FLOOR CHICAGO, IL 60606			EXAMINER FORD, VANESSA L	
			ART UNIT 1645	PAPER NUMBER
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		01/30/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/673,054	Applicant(s) ENGEL ET AL.	
	Examiner Vanessa L. Ford	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 October 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28, 67-77, 79 and 122-125 is/are pending in the application.
- 4a) Of the above claim(s) 4, 5 and 13-15 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 125 is/are allowed.
- 6) ☒ Claim(s) 1-3, 6-12, 16-28, 67-77, 79 and 122-124 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

FINAL ACTION

1. This action is in response to Applicant's remarks filed October 30, 2006.
2. The text of those sections of the Title 35, U.S. code not included in this action can be found in the prior Office Action.

Rejection Maintained

3. The rejection under 35 U.S.C. 103(a) paragraph is maintained for claims 1-3, 6-12, 16-28, 67-77, 79 and 122-124 for the reasons set forth on pages 3-9, paragraph 5 of the previous Office Action.

The rejection was on the grounds that Chu et al teach compositions comprising aqueous solutions of alkylglycoside or alkylthioglycoside, particularly (octylthiogluconate) (columns 1-2). Chu et al teach that the octylthiogluconate used in the compositions range from about 0.5 to about 5% w/v (column 2-3). Chu et al teach that the octylthiogluconate can be included in an aqueous solution at about 0.5% (v/w) to about 5% (v/w) (column 3). This meets the claims limitations "...at least 0.4% and less than 1% (w/v)" and "...between 0.4% and 0.6% (w/v). Chu et al teach that buffers such as TRIS or HEPES can be added to the compositions to maintain a physiological pH of about 7-8 (column 2). Chu et al teach that the buffers can be maintained at a pH of 7.5 (column 3, Example II). Chu et al teach that lysozyme (reduces non-specific binding) can be added to the compositions (column 24, Example 4). Chu et al teach that the invention was used to prepare, extract, detect, purify and collect the isolated proteins (see Examples I-V, columns 3-6). Chu et al teach that the protein products are incubated on Nickel charged resins (magnetic) and further purified using spin columns comprising resins (Example V, columns 5-6). Chu et al teach compositions comprising aqueous solutions of octylthiogluconate used for lysing cells in the protein extraction process (columns 1-2) and Chu et al teach that the octylthiogluconates of the invention can release the protein of interest from the cell membrane or cell wall (column 2). Chu et al also teach that octylthiogluconates have been used for membrane solubilization (column 2). Therefore, claim limitations such as "wherein the cell altering compound inhibits phospholipid sensitive Ca⁺² dependent protein kinase and attacks cell membranes" and "cell membrane compounds alters membrane permeability or disrupts membranes" are taught in the prior art reference.

Chu et al do not teach cationic surfactants(elected species).

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Shultz et al teach that cationic surfactants such as Tomah E –18-15 or Tomah E-18-5 are used to stabilize protein compositions (see the Abstract). Shultz et al teach that the cationic surfactants of the invention have a hydrophile-lipophile (HLB) index number of about 10 to 17, preferably about 11 to 16 (column 2). Shultz et al teach that cationic surfactants such as Tomah E –18-15 or Tomah E-18-5 can be used to stabilize proteins in both storage buffers and reaction enzymes (column 8). Shultz et al teach that the cationic surfactants can be added at concentrations ranging from 0.001% up to 1.0% (column 11). In re Venezia 189 USPQ 49 (CCPA 1976) discloses kits are drawn to the structural attributes of interrelated component parts and not to activities that may or may not occur. Thus, the term “kit” constitutes an “intended use”. Intended use does not impart patentable weight to a product. See MPEP 2111.03: Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In re Casey, 370 F.2d 576, 152 USPQ 235 (CCPA 1967); In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963).

It would be *prima facie* obvious at the time the invention was made to add Tomah E –18-15 and/or Tomah E-18-5 to aqueous solutions of Chu et al comprising octylthioglucosides because Shultz et al teach that cationic surfactants such as Tomah E –18-15 or Tomah E-18-5 can be used to stabilize proteins in both storage buffers and reaction enzymes in solution (see the Abstract and column 8). It would be expected barring evidence to the contrary that a composition comprising octylthioglucosides (cell-altering membrane), Tomah E –18-15 and/or Tomah E-18-5 (cationic surfactant), lysozyme (defoaming agent) and HEPES (buffer salt) would be effective in lysing cells to release proteins and stabilizing the proteins in reaction or storage buffers.

Applicant's Arguments

A) Applicant urges that Shultz et al do not suggest that detergents of any type in the HLB range of about 11-16 and is limited to cationic surfactants. Applicant urges that there is no incentive to select any surfactant in this HLB range in order to provide the composition or method of the present invention as presently claimed.

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B) Applicant urges that Shultz et al do not actually teach or suggest cell lysis nor does she teach or suggest that this would be necessary or desirable to do. Applicant urges that selection of a material such as a surfactant to provide enzyme stability does not automatically presume that it will also provide effective lysis. Applicant urges that some surfactants can form micelles that may act to provide additional stabilization of cellular membrane proteins, thus making extraction more difficult. Applicant urges that one of ordinary skill in the art would not be motivated by the teachings of Shultz et al concerning protein stabilization to include a surfactant in Chu et al lysis reagent and thus arrive with the presently claimed invention with any reasonable expectation of success.

C) Applicant urges that a prima facie case of obviousness has not been established because the instant application disclosed unexpected results for the claimed composition that are not taught or suggested in either of these references alone or in combination.

D) Applicant urges that example 18 discloses a comparison between solution (octyl-beta-thioglucopyranoside only) with solution 3 ((octyl-beta-thioglucopyranoside, triton X-100 and Tomah E-18-15). Applicant urges that the application has demonstrated that cells treated with the combination of cell membrane altering polymyxin B and the surfactant produced a surprising enhanced luciferase activity in the supernatant relative to the results obtained from cells treated with the cell membrane altering compound alone.

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Applicant urges that example 17 compares the results of a cell membrane altering compound alone with a combinations of cell membrane altering compounds with a surfactant. Applicant urges that the combined teachings of Chu et al and Shultz et al either alone or in combination do not teach or suggest the surprising results obtained by the claimed invention.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed October 30, 2006 have been fully considered but they are not persuasive.

A) The Examiner disagrees with Applicant's assertions that "that Shultz et al do not suggest that detergents of any type in the HLB range of about 11-16 and is limited to cationic surfactants and there is no incentive to select any surfactant in this HLB range in order to provide the composition or method of the present invention as presently claimed". Shultz et al teach that cationic surfactants such as Tomah E -18-15 or Tomah E-18-5 are used to stabilize protein compositions and further teach that the cationic surfactants of the invention have a hydrophile-lipophile (HLB) index number of about 10 to 17, preferably about 11 to 16 (column 2). It should be noted that no method claims are pending in the present application.

B) To address Applicant's comment regarding stability and effective lysis of surfactants, it should be noted that Shultz et al teach that Tomah E –18-15 or Tomah E-18-5 (surfactants) can be used to stabilize proteins and Chu et al teach that octylthioglucosides (cell membrane altering compound) used for lysing cells. Therefore, it should be remembered that it is the combination of all of the cited and relied upon references which make up the state of the art with respect to the claimed invention. Thus, one of ordinary skill in the art would expect success when combining the prior art reference to arrive at the claimed invention.

C) In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the claims are directed to a composition comprising at least one surfactant having a lipophilic balance value in the range of about 11 to about 16 and at least one cell membrane altering compound. Chu et al teach compositions comprising aqueous solutions of octylthioglucoside used for lysing cells in the protein extraction process and further teach that the octylthioglucosides (cell membrane altering compound) of the invention

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can release the protein of interest from the cell membrane or cell wall. Chu et al do not teach cationic surfactants comprising ethoxylated amine such as Tomah E -18-15 or Tomah E-18-5 (see the Abstract and column 1). Chu et al teach that other constituents which do no adversely effect the use and benefits of the solution can be added to the invention such as buffers or constituents that influence by the protein that is being expressed (column 2). However, Shultz et al teach that cationic surfactants such as Tomah E -18-15 or Tomah E-18-5 are used to stabilize protein compositions (see the Abstract and columns 1-2). One of ordinary skill in the art would be motivated to add Tomah E -18-15 and/or Tomah E-18-5 to aqueous solutions of Chu et al comprising octylthioglucosides because Shultz et al teach that cationic surfactants such as Tomah E -18-15 or Tomah E-18-5 can be used to stabilize proteins in both storage buffers and reaction enzymes in solution. One ordinary skill in the art would reasonably conclude that the addition cationic surfactants such as Tomah E -18-15 or Tomah E-18-5 would provide a stable aqueous solution.

To address Applicant's comments regarding unexpected results, it should be remembered that MPEP at section 2112.01 states "products of identical chemical composition can not have mutually exclusive properties". Thus, the compositions obtained by combining the prior art teachings would have the same unexpected characteristics as the claimed composition.

D) While example 17 discloses release of protein from E. coli cells using a second cell permeabilization reagent (octyl-beta-thioglucopyranoside) and example 18 discloses that the addition of protein stabilization detergents to solutions of octyl-beta-thioglucopyranoside can produce a solution that is not as damaging to protein activity as solutions not containing the stabilizing chemicals, it should be remembered that the combination of prior art references teach the claimed invention.

As stated above, one of ordinary skill in the art would be motivated to combine the prior art references because to add Tomah E -18-15 and/or Tomah E-18-5 to aqueous solutions of Chu et al comprising octylthioglucosides because Shultz et al teach that cationic surfactants such as Tomah E -18-15 or Tomah E-18-5 can be used to stabilize proteins in both storage buffers and reaction enzymes in solution. It should be noted that Chu et al teach that other constituents which do not adversely effect the use and benefits of the solution can be added to the invention such as buffers or constituents that influence by the protein that is being expressed (column 2). Schultz et al provides constituents such as Tomah E -18-15 and/or Tomah E-18-5 which can be used to enhance the stability of aqueous solutions. Thus, the composition that the artisan of ordinary skill would arrive at by combining the prior art teachings would have necessarily have the same unexpected results as possessed by the claimed composition.

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In view of all of the above, there is nothing on the record to show that the combination of teachings would not suggest the claimed invention. Therefore, the rejection is maintained.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.


JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

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In view of all of the above, there is nothing on the record to show that the combination of teachings would not suggest the claimed invention. Therefore, the rejection is maintained.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Status of Claims

5. Claim 125 is allowed. The closest prior art is Shultz et al (*U.S. Patent No. 6,242, 235 published June 2001*) and Chu et al (*U.S. Patent No. 6,174, 704 published January 16, 2001*). Shultz et al teach cationic surfactants Tomah and Triton but do not teach compositions comprising 2% Tomah and 2% Triton X100 and the cell membrane altering compound octyl beta thioglucopyranoside at 6% in 500 mM HEPES at pH 7.5. Chu et al (*U.S. Patent No. 6,174, 704 published January 16, 2001*) teach compositions comprising octyl beta thioglucopyranoside but does not teach compositions comprising 6% octyl beta thioglucopyranoside in 500 mM HEPES at pH 7.5 and surfactants 2% Tomah and 2% Triton X100.

Conclusion

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vanessa L. Ford whose telephone number is (571) 272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery Siew can be reached on 571.272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Vanessa L. Ford
Biotechnology Patent Examiner
January 16, 2007